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(54) Title: VIGILANT CELLS

(57) Abstract: Bone marrow-derived mesenchymal stem cells were transduced with a stimulus-responsive rAAV vector system that detects and responds to hypoxia in cardiac tissue. A first rAAV vector in the system contains a cardiac-specific promoter linked to a sequence encoding an oxygen-sensitive chimeric transactivator containing a GAL4 DNA binding domain, an oxygen-dependent degradation domain, and a p65 activation domain. A second rAAV vector contains a cardioprotective gene linked to a GAL4 UAS. The first rAAV vector expresses the chimeric transactivator specifically in the heart, and in response to hypoxia, the transactivator binds to the GAL4 upstream activating sequence (UAS) in the second rAAV vector. Binding of the transactivator to the UAS results in the expression of the cardioprotective gene. The rAAV vectors can be used to treat cells in a number of other disease states, including diabetes, cancer, stroke, and atherosclerosis. These approaches to stem cell-based gene therapy provide a novel strategy not only for treatment but for prevention of cell destruction.